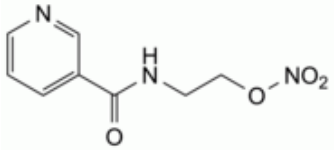
Edition: BP 2025 (Ph. Eur. 11.6 update)

Nicorandil

General Notices

(Ph. Eur. monograph 2332)



$C_8H_9N_3O_4$ 211.2 *65141-46-0*

Action and use

Potassium channel opener.

Preparation

Nicorandil Tablets

Ph Eur

DEFINITION

2-[(Pyridin-3-ylcarbonyl)amino]ethyl nitrate.

Content

99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Sparingly soluble in water, freely soluble in anhydrous ethanol, practically insoluble in heptane.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison nicorandil CRS.

TESTS

pH (2.2.3)

5.5 to 7.0.

Dissolve 0.25 g in carbon dioxide-free water R and dilute to 25 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29). *Prepare the solutions immediately before use.*

Test solution Dissolve 50 mg of the substance to be examined in the mobile phase and dilute to 25.0 mL with the mobile phase.

Reference solution (a) Dissolve 2 mg of nicorandil impurity A CRS in the mobile phase using sonication and dilute to 25.0 mL with the mobile phase. Dilute 1.0 mL of the solution to 20.0 mL with the test solution.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography compatible with 100 per cent aqueous mobile phases R (5 µm).

Mobile phase trifluoroacetic acid R, triethylamine R, tetrahydrofuran R, water R (3:5:10:982 *V/V/V/V*).

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 10 µL.

Run time 1.5 times the retention time of nicorandil.

Identification of impurities Use the chromatogram obtained with reference solution (a) to identify the peak due to impurity A.

Relative retention With reference to nicorandil (retention time = about 19 min): impurity A = about 0.9.

System suitability Reference solution (a):

— resolution: minimum 2.5 between the peaks due to impurity A and nicorandil.

Calculation of percentage contents:

— for each impurity, use the concentration of nicorandil in reference solution (b).

Limits:

— *unspecified impurities*: for each impurity, maximum 0.10 per cent;

— *total*: maximum 0.2 per cent;

— *reporting threshold*: 0.05 per cent.

Sulfates (*2.4.13*)

Maximum 100 ppm.

Dissolve 5.000 g in 30 mL of *ethanol (50 per cent V/V) R*, add 1 mL of *dilute hydrochloric acid R* and dilute to 50.0 mL with *distilled water R*.

Water (*2.5.32*)

Maximum 0.5 per cent.

Dissolve 0.300 g in a suitable solvent and dilute to 1.0 mL with the same solvent. Inject 0.400 mL of the solution through the septum.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.150 g in 50 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

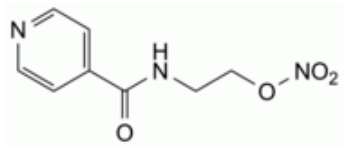
1 mL of *0.1 M perchloric acid* is equivalent to 21.12 mg of $C_8H_9N_3O_4$.

STORAGE

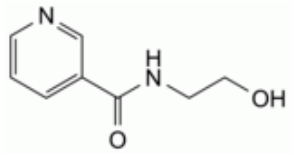
At a temperature of 2 °C to 8 °C.

IMPURITIES

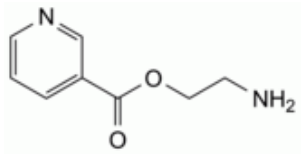
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use) A, B, C, D.



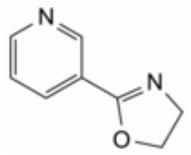
A. 2-[(pyridin-4-ylcarbonyl)amino]ethyl nitrate,



B. *N*-(2-hydroxyethyl)pyridine-3-carboxamide,



C. 2-aminoethyl pyridine-3-carboxylate,



D. 3-(4,5-dihydro-1,3-oxazol-2-yl)pyridine.

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